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RESEARCH ARTICLE

Identification of seniors at risk (ISAR) score and potentially inappropriate prescribing: a retrospective cohort study

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Abstract

Background Potentially inappropriate prescribing (PIP) is usually associated with a higher risk of adverse health outcomes. It is therefore important to identify PIP in older adults. However, there are no clear prioritisation strategies to select patients requiring prescription reviews.

Aim The aim of this study was to assess the association between the identification of seniors at risk (ISAR) score and the number of PIPs.

Method A 12-month retrospective hospital-based study was conducted. PIPs, including potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs), were detected using the STOPP/START tool. Multivariate linear regressions were conducted to identify factors associated with the number of PIPs. Sensitivity, specificity, Youden index, and ROC curve were calculated to determine the predictive power of ISAR score.

Results This study included 266 records. The analysis led to the detection of 420 PIMs and 210 PPOs, with a prevalence of 80.1% and 54.9%, respectively. Multivariate linear regression revealed that the ISAR score ($p=0.041$), and the number of medications ($p<0.001$) were determinants of PIP. The number of medications remained the sole determinant of the number of PIMs ($p<0.001$), while living in a nursing home was the only determinant of the number of PPOs ($p=0.036$).

Conclusion The study showed that the ISAR score and the number of medications were independently associated with the number of PIPs. Considering the use of the ISAR score and the number of medications may be useful strategies to prioritise patients for whom prescribing appropriateness should be assessed using explicit criteria.

Keywords Aged · Polypharmacy · Potentially inappropriate prescribing · STOPP/START criteria

Impact statements

- The ISAR score can be used as a selection criterion for prescribing appropriateness analysis.
- Efforts must be made to reduce prescriptions for benzodiazepines, aspirin, and proton-pump inhibitors, which are often inappropriate.

Introduction

Medications are generally well tolerated in the general adult population. However, this is not always the case for older people, as age-related changes in pharmacokinetics and pharmacodynamics can modify the benefit-risk balance of a medication [1, 2]. Potentially inappropriate prescribing (PIP) encompasses potentially inappropriate medication (PIM) i.e., the prescription of a medication with a negative benefit-risk ratio, and potential prescribing omission (PPO) i.e., the omission of prescribing a medication with potential benefit in the prevention or treatment of a disease [3]. The presence of PIPs is a significant health concern for older patients, as it increases the risk of adverse drug events and related outcomes such as hospitalisation or death [4, 5] Developing tools to help practitioners identify these PIPs is essential. Several tools can be used to assess the appropriateness of prescribing for older adults based on implicit criteria,

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such as the Medication Appropriateness Index (MAI) [6], or explicit criteria, such as the AGS Beers criteria [3, 7].

The Screening tool of older person's prescriptions (STOPP) and the Screening tool to alert doctors to right treatment (START) are tools that use explicit criteria to identify PIM and PPO, respectively, in patients aged 65 years and older. Published in 2008 following validation through a Delphi consensus process, the tools initially included 65 STOPP criteria and 22 START criteria [8]. These tools have been subsequently updated twice using the same validation process. The first update occurred in 2015, increasing the number of STOPP criteria to 80, and the number of START criteria to 34 [9]. The second update occurred in 2023, resulting in the current number of 133 STOPP criteria and 57 START criteria [10].

Potentially inappropriate prescribing is common among older hospitalised patients, with a PIM prevalence ranging from 23 to 77% and a PPO prevalence ranging from 51 to 73% [11]. Furthermore, the probability of having PIP is greater after hospitalisation than before [12]. Therefore, it is crucial to systematically identify PIP in older hospitalised patients. This task is often hindered by the current lack of systematic procedures, mainly due to time constraints [13]. Some studies have tried to identify prioritisation strategies. For example, Cullinan et al. [14] proposed the use of a frailty index as a clinical indicator of the presence of PIP in older adults. Jovevski et al. [15] used the identification of seniors at risk (ISAR) to select high-risk geriatric patients for a pharmacist-led medication reconciliations. The reconciliations were specifically targeted towards identifying PIMs and providing deprescribing recommendations to the patients' primary care provider.

The ISAR screening tool was developed in 1999 by McCusker et al. [16] to detect, in the emergency department (ED), older people at increased risk of adverse health outcomes, including functional decline, unplanned hospitalisation or ED visit, institutionalisation or death. Initially developed for the ED, it is now widely used to assess hospitalised inpatients [17]. The tool is composed of six self-reported closed questions (need for help in activities of daily living; an increase in this need related to the current illness; hospitalisation in the previous 6 months; significantly altered vision; memory problems; and daily use of ≥ 3 medications at home). Each question is scored 1 if the patient answers 'yes' and 0 otherwise, resulting in a scale ranging from 0 to 6. A score of 2 or more indicates an increased risk of adverse health outcomes [16]. It is one of the most frequently used tools for assessing functional decline [18].

Aim

The aim of this study was to assess the potential association between the ISAR score and the number and type of PIPs. The secondary objective was to determine the ability of the ISAR score to predict the presence of inappropriate prescribing.

Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Ambroise Paré Hospital on August 24, 2022, with the approval reference number HAP-2022-044.

Method

Study design and population

We conducted a 12-month retrospective study (January 2021–December 2021) based on the medical records of patients hospitalised in the cardio-neurological service (0H) of a teaching hospital in Mons, Belgium. This service was selected because it covered a heterogeneous population, and an ISAR score was systematically calculated for all patients aged 75 years or older upon admission. The score was only calculated for individuals below this age if there was a suspected decline. Therefore, we excluded patients under 75 years old as they were more likely to have a positive ISAR score if it was available. Inclusion criteria were having an available ISAR score, taking at least one medication, and having a medical history in the hospital. Records with missing data or from patients re-hospitalised in the same year were excluded.

Data collection

Sociodemographic (age, gender, family status), biological (weight, glomerular filtration rate (GRF), plasma sodium, potassium, and calcium concentration), clinical (disease, reason of hospital admission, ISAR score), and medications data were collected from electronic patient records. Family status was categorised into four groups: alone at home, with a partner at home, with family at home, and in a nursing home residence (NHR).

Polypharmacy and indicators of PIP

Medications were reported using the international non-proprietary name (INN). Polypharmacy was defined as the presence of five or more chronic medications, and hyper-polypharmacy was defined as the presence of ten or more chronic medications [19]. PIPs were assessed using the French version of the STOPP/START tool version 2 [20]. Out of the 114 criteria from the original tool, 5 STOPP and 5 START criteria had to be adapted due to the retrospective

context of the study. The changes can be found in Supplementary Material 1. The treatments and comorbidities of each patient were analysed by the first researcher (SL) to determine the PIPs. The obtained results were verified by a second researcher (JB). In cases of disagreement, the two researchers conducted a discussion to reach a consensus. If consensus could not be reached after the discussion, a third researcher (SP) made the final decision.

Statistical analysis

Continuous data are reported using the mean with standard deviation, while categorical variables are reported using numbers and percentages. Normality of continuous data was performed using a combination of the Kolmogorov–Smirnov test and graphical interpretation. The distribution of categorical variables was compared using Pearson's chi-square test (χ^2), and the independent Student's t-test was used for continuous variables. For categorical variables that were present in more than two groups, ANOVA followed by Bonferroni post hoc analysis was used. Three multivariate linear regression analyses were employed to identify the determinants of PIP. The number of PIPs was the dependent variable of the first regression, while the number of PIMs and the number of PPOs were the dependent variables of the second and the third regressions, respectively. Categorical variables with more than two options were coded using a dummy coding system. The accuracy of the ISAR score to discriminate the presence of at least one PIP was evaluated using sensitivity, specificity, and the area under the receiver operating characteristic (ROC) curve. The Youden index was used to determine the optimal discriminatory performance cut-off. Statistical analyses were performed using IBM® SPSS Statistics version 26. A p value of < 0.05 was considered statistically significant.

Results

Characteristics of the study population

Out of the initial 1181 records that the 0H service had for the year 2021, 672 were excluded due to patient age (< 75 years), 181 were excluded due to missing data, and 62 were excluded as they were records of re-hospitalised patients. This resulted in a total of 266 records being included in the study. The flowchart of the inclusion process is presented in Fig. 1. Patients were mostly women (53.8%), and the mean age was 82.8 years (SD 5.5). Most of them lived alone at home (39.1%) or with a partner at home (38.3%). Patients had a mean ISAR score of 2.75 (SD 0.09). Patients were found to be taking a mean of 7.9 chronic medications (SD 3.4). Polypharmacy was observed in 55.2% of the study population and hyper-polypharmacy was observed in 30.1%. Further details of the study population are presented in Table 1.

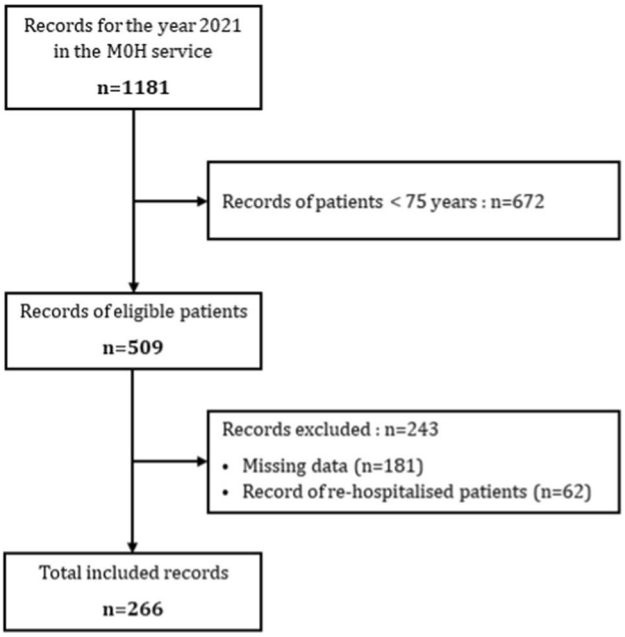

Fig. 1 Flowchart of the records selection process

Prevalence of PIP

A very high percentage of the population had at least one PIP (90.2%). Regarding PIM and PPO, 80.1% of the study patients had at least one STOPP criterion, and 54.9% had at least one START criterion. The STOPP criteria identified 420 PIMs, while the START criteria identified 210 PPOs, resulting in a total of 620 PIPs. Over 50% of PIMs concerned three drug classes: benzodiazepines (22.4%), aspirin (20.2%) and Proton-Pump Inhibitors (12.4%). No medical condition was overrepresented for PPOs. The first three were ischaemic cardiopathy (11.4%), persistent hypertension (11.0%), and falls, osteopenia, or confinement (10.0%). The complete list can be found in Supplementary Material 2.

Factors related to PIP

Multivariate linear regression analysis revealed that the ISAR score, and the number of chronic medications were independent determinants of the number of PIPs ($p = 0.041$ and $p < 0.001$, respectively). The beta coefficient showed that the number of PIPs increases by 0.12 when the ISAR score increases by 1 and the number of PIPs increases by 0.21 for every additional chronic medication. When considering only the STOPP criteria, the number of chronic medications was the sole determinant of the number of PIMs ($p < 0.001$), with

Table 1 Characteristics of the study population

Characteristic	Value	No PIP (25)	At least one PIP (241)
Age, mean (SD[1])	82.8 (5.5)	81.8 (6.3)	82.9 (5.4)
Gender, n (%)			
Female	143 (53.8)	10 (40.0)	133 (55.2)
Male	123 (46.2)	15 (60.0)	108 (44.8)
Family status, n (%)			
Alone at home	105 (39.4)	10 (40.0)	94 (39.0)
With a partner at home	101 (38.0)	14 (56.0)	88 (36.5)
With family at home	33 (12.4)	1 (4.0)	32 (13.3)
In nursing home residence	27 (10.2)	–	27 (11.2)
ISAR score, n (%)			
0	14 (5.3)	2 (8.0)	12 (5.0)
1	48 (18.0)	7 (28.0)	41 (17.0)
2	62 (23.3)	6 (24.0)	56 (23.2)
3	56 (21.1)	3 (12.0)	53 (22.0)
4	48 (18.0)	5 (20.0)	43 (17.9)
5	28 (10.5)	1 (4.0)	27 (11.2)
6	10 (3.8)	1 (4.0)	9 (3.7)
ISAR score, mean (SD)	2.75 (0.09)	2.4 (1.6)	2.8 (1.5)
Medication, n (%)			
No polypharmacy	39 (14.7)	11 (44.0)	28 (11.6)
Polypharmacy	146 (54.9)	14 (56.0)	133 (55.2)
Hyper-polypharmacy	81 (30.4)	–	80 (33.2)
No. of medications, mean (SD)	7.9 (3.4)	5.1 (2.6)	8.2 (3.4)
PIP, mean (SD)	2.37 (1.55)	–	2.61 (1.42)
STOPP criteria (PIM)	1.58 (1.23)	–	1.74 (1.18)
START criteria (PPO)	0.79 (0.88)	–	0.87 (0.89)

[1] *SD* standard deviation

a beta coefficient of 0.19. For START criteria, the family status was the only factor determining the number of PPOs ($p = 0.011$), with a beta coefficient of 0.12. For the whole result of the regression, see Table 2. An ANOVA followed by a Bonferroni post-hoc analysis showed that patients living in an NHR had significantly more PPOs than the other patients ($p = 0.013$).

Performance of the ISAR score

The area under the ROC curve for the ISAR score was 0.58 (Fig. 2). For a cut-off of ≥ 2, the sensitivity was 0.78 and the specificity was 0.36, with a Youden index of 0.14. The sensitivity and specificity for each cut-off are presented in Table 3.

Table 2 Results of the multivariate linear regression for PIP, PIM and PPO

Factors	PIP		STOPP criteria		START criteria	
	B[a]	*p* value	B	*p* value	B	*p* value
Gender	−0.191	0.701	−0.133	0.302	−0.058	0.591
Age	0.012	0.420	0.011	0.348	0.001	0.914
Family status	0.077	0.388	−0.046	0.515	0.123	**0.036**
ISAR score	0.118	**0.041**	0.054	0.235	0.065	0.087
No. of medications	0.211	**< 0.001**	0.192	**< 0.001**	0.020	0.225

[a] B: non-standardised coefficient. Bold text represents statistically significant *p* values

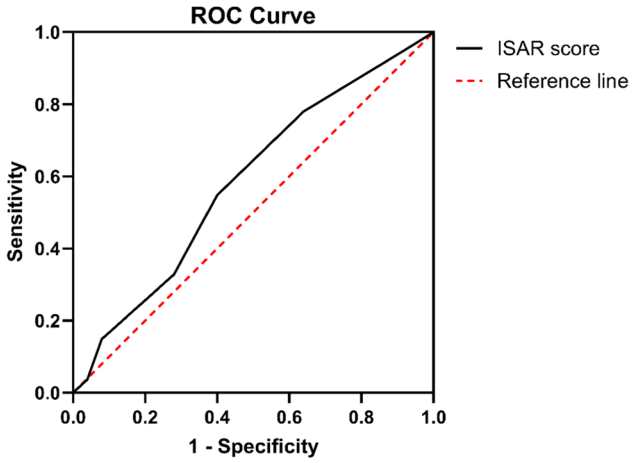

Fig. 2 ROC curve for the ISAR score

Table 3 Sensitivity, specificity, and Youden index for each cut-off of the ISAR score

Cut-off	Sensitivity	Specificity	Youden index
≥ 1	0.95	0.08	0.03
≥ 2	0.78	0.36	0.14
≥ 3	0.55	0.60	0.15
≥ 4	0.33	0.72	0.05
≥ 5	0.15	0.92	0.07
≥ 6	0.04	0.96	0.00

Discussion

Statement of key findings

Our study showed that the ISAR score and the number of chronic medications were independently associated with the number of PIPs. This number increases by 12% for each additional point on the ISAR score, and by 21% for each additional chronic medication. However, when PIM and PPO were examined separately according to the STOPP and START criteria, the relationship with the ISAR score disappeared, indicating that the relationship was due to the STOPP and START criteria as a whole. The number of medications remained a predictor for the number of PIMs, but not for the number of PPOs. Family status was identified as the only predictor of the number of PPOs. Three drug classes (aspirin, benzodiazepine, and proton-pump inhibitors) had a significantly higher number of related PIM than the other classes. This highlights the need to pay particular attention to these three drug classes when prescribing.

Interpretation

This study confirmed that an increased number of medications is associated with a higher risk of PIM, as previously described by Dalleur et al. [21], Martinot et al. [22], and Steinman et al. [23]. This association was observed regardless of the list of explicit criteria used in the studies; the French Laroche list, the Beers list, and the STOPP/START (v1 and v2) were the most used lists. The relationship between the number of medications and PPO is less clear. While some studies, such as Gutiérrez-Valencia et al. [24] and Hanna et al. [25], have shown that polypharmacy is a predictor of the presence of PPO, others, such as Dalleur et al. [21] and Steinman et al. [23] have not found any association between PPO and the number of medications. These conclusions are the same as those of our study. This observed difference may be attributed to the difference in the populations studied. Studies showing a correlation are usually conducted with older adults living in the community, whereas those that do not show a correlation are based on hospital populations. Further research is necessary to clarify this point. However, a correlation between the number of PPOs and family status, particularly among institutionalised patients, has been established. These findings support previous research indicating that institutionalised patients are at higher risk of PPO [24, 26]. This significantly higher risk of having PPO can be explained by the interpretation of one of the START criteria in our study. The START criterion "falls, osteopenia, confinement" was considered present if a patient living in an NRH had no vitamin D in their medication, as we considered those patients to be confined. Moreover, upon removing this criterion from the analysis, the correlation between family status and the number of PPOs disappeared, indicating that it was mainly responsible for the association between the latter two.

In our study, 90.2% of the patients presented at least one PIP, which is much greater than the mean prevalence of 34.6% reported in a recent systematic review [27]. Similarly, the prevalence of PIM was also higher, with 80.1% in our study compared to the mean of 35% reported for Europe in a meta-analysis [28]. Such a difference is not uncommon and can be attributed to the heterogeneity between studies in terms of inclusion and exclusion criteria, context, and health status. Brkic et al. [27] explained in their review that differences in health and social care systems between countries can also contribute to these variations. However, benzodiazepine and proton-pump inhibitors were among the three most frequently identified PIM in our study, consistent with the findings of Tian et al.'s systematic review and meta-analysis [28]. Although we did not find any systematic review about the prevalence of PPOs, a study conducted between 2015 and 2019 using START criteria version 2 found a prevalence

of 58% in a population of older hospitalized patients [29]. Our finding of a prevalence of 54.9% is consistent with this.

Implementing interventions to reduce PIPs is a time-consuming process. Therefore, proposing a strategy based on a tool that is already implemented in several hospitals may be interesting. To identify patients at highest risk of PIP, our study suggests using the ISAR score and the number of medications as selection criteria for evaluating the appropriateness of prescribing. Patients with a high ISAR score and a high number of medications should be prioritised for evaluation based on an explicit criteria list. To the best of our knowledge, no published study has compared the number of PIPs to the ISAR score. Some studies, such as those conducted by Dalleur et al. [21] or Salm et al. [30], used the ISAR score as an inclusion criterion, where patients had to have a score ≥ 2 to be included in the study. In the study of Salm et al., although patients had to have an ISAR score ≥ 2, it is possible to observe that patients with more than 4 PIPs had a higher ISAR score than those with 4 PIPs or less. However, this difference was not statistically tested [30]. As shown in the literature, the ISAR score is predominantly employed with a cut-off value, whether to identify patients at risk of adverse health outcomes [16] or frail patients [31]. It would therefore be tempting to propose such a threshold for prioritising patients requiring a medication review. Using a cut-off of ≥ 2, as originally proposed [16], would give a sensitivity of 78% and a specificity of 36%. However, as demonstrated by linear regression, the higher the ISAR score is, the more PIPs patients will have. Moreover, the area under the ROC curve obtained (0.58) is close to 0.5, indicating a low-performance marker. It would therefore be more appropriate to propose a priority ranking rather than limiting the analysis to a cut-off value. In this case, a score of 6 would indicate a high priority for a medication review, while a score of 0 would indicate a low priority.

Strengths and weaknesses

This is the first study to evaluate the potential use of the ISAR score as a predictor of the presence of PIP, offering new perspectives for a widely used tool. However, our study has some limitations. First, the study was monocentric and conducted on a specific hospitalised population making it difficult to extrapolate the findings to other populations. Secondly, the records were consulted retrospectively. Therefore, we were unable to consult patients or physicians to verify or complete the data.

Further research

Further research is required to evaluate the performance of the ISAR score in the prediction of the presence of PIP through robust statistical analyses. Further studies are also necessary to investigate the potential strategy of using the ISAR score and the number of medications to prioritize patients requiring prescription review. It is important to determine if this approach adds value to the care of older hospitalised patients.

The determination of PIP was made using STOPP/START version 2. It is worth noting that the tools have been updated and now contain 53 new STOPP criteria and 23 new START criteria as well as new categories in the START tool [10]. As the updated lists were not published at the time of the study, the methodologies should be repeated using the latest version of the lists.

Conclusion

We successfully established an association between the ISAR score and the number of PIPs, indicating that the ISAR score could be used for prioritising patients requiring prescription reviews. This approach is particularly useful because the ISAR score is already widely used in hospitals. Furthermore, our results confirm that the number of PIPs increases with the number of medications. Consequently, the number of chronic medications taken by the patient provides additional support for prioritisation.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11096-024-01766-2.

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Conflicts of interest The authors declare no conflict of interests.

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